REMARKS

Claims 1-48 are pending, and claims 8-11, 13, 17, 18, 20, 37-41, 43, 46 and 48 are under examination. Claims 1-7, 12, 14-16, 19, 21-36, 42, 44, 45 and 47 have been withdrawn. In this Amendment, applicants have amended claim 8, and have cancelled claims 1-7, 9-12, 14-16 and 18-48. Applicants maintain that these changes raise no issue of new matter. Upon entry of this Amendment, claims 8, 13 and 17 will still be pending and under examination.

35 U.S.C. §101

The Examiner rejected claims 8-11, 18 and 37-41 under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter. Specifically, the Examiner stated that the claimed antibodies are naturally occurring. The Examiner also stated that the rejection could be overcome by amending the claims to indicate that the antibodies are isolated.

In response, applicants note that claim 8 has been amended per the Examiner's recommendation, thus indicating that the claimed antibody is essentially free of other antibodies. Applicants have therefore obviated the rejection. As for the remaining rejected claims, applicants note that their cancellation renders the rejection thereof moot.

35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 8-11, 13, 17, 37, 38 and 48 under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

The Examiner objected to the inclusion of both SEQ ID NO:1 and SEQ ID NO:5 in claim 8 as allegedly unclear. In response, applicants note that claim 8, as amended, recites only SEQ ID NO:5. Applicants maintain that amended claim 8 satisfies the requirements of 35 U.S.C. §112, second paragraph.

The Examiner also noted objectionable language in claims 37 and 38. Without conceding the correctness of the Examiner's remarks, applicants note that the claims have been cancelled, rendering their rejection moot.

35 U.S.C. §112, First Paragraph

The Examiner rejected claims 17, 46 and 48 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. Claims 46 and 48 have been cancelled, rendering their rejection moot.

In response to the rejection of claim 17, applicants respectfully traverse.

Claim 17 provides a vaccine to treat a patient with severe acquired respiratory syndrome or prevent the onset thereof, comprising an effective amount of the antibody of claim 8.

The Examiner states that although the specification teaches that some antibodies neutralize virus infectivity in cultured cells, there is no working example showing successful treatment or prevention of disease. The Examiner goes on to state that the "prior art contains conflicting evidence on the efficacy of neutralizing antibodies to treat or prevent other coronavirus diseases, and contemporary uncertainty on which of the coronaviruses (if any) provide a reasonably [sic] model for SARS." Finally, the Examiner notes the "extraordinary virulence" of SARS infection, and asserts that those skilled in the art would require "extensive guidance" in administering the antibody. Thus, according to the Examiner, undue experimentation would be required.

Applicants point out the following in response to these assertions by the Examiner.

To reiterate, the invention of claim 17 is a vaccine comprising the antibody of claim 8. That antibody, in turn, is directed to the neutralizing fragment of the spike (S) gene of SARS CoV, clone 12 of the 2774 strain (SEQ ID NO:5), corresponding to amino acid residues 1055-

1192. Accordingly, any discussion of enablement must focus on this particular vaccine comprising this particular antibody, rather than SARS vaccines generally.

Also as stated at p. 11, lines 16-24 of the application, applicants' "results showed that the 48-1055 aa of S protein is less suitable for ... vaccines ... [and that]... it is clear that the region 1055 to 1192 aa of S protein SEQ ID NO. 5 contains linear epitope(s) that *would* be suitable for subunit vaccine development." (emphasis added).

Further, it is not necessary that the application provide working examples showing actual therapeutic results using the claimed vaccine. Rather, it must simply be that no *undue* experimentation would be required to practice the invention. The need for experimentation does not negate enablement, so long as the experimentation is not undue.

Again, the Examiner asserts a lack of suitable SARS models among other carovaviruses, and the conflicting evidence on the efficacy of neutralizing antibodies in treating disorders other than SARS, citing Saif and Cavanaugh in support of this position.

Briefly, applicants note that Saif was published a decade prior to applicants' filing date, and thus does not properly represent the art at the time of filing. Having said that, applicants also note that even at the time of the Saif reference, the passive transfer of virus-neutralizing antibodies against -- in relevant part -- the S glycoprotein conferred passive protection against coronavirus challenge in "some studies, but not others." (See Abstract). This outcome indicates that passive protection has been achieved, although not in all cases. Together with the subject invention, the Saif reference does not properly support the conclusion that undue experimentation would be needed to confer passive protection using the subject vaccine.

As for Cavanaugh, this reference appears to address vaccines involving viral proteins *per se* (e.g., in the form of killed virus), rather than vaccines comprising neutralizing antibodies. Hence, this reference is of questionable relevance regarding enablement of the claimed vaccine.

Importantly, applicants bring to the Examiner's attention the following references, which strongly indicate the claimed vaccines' likely success, and thus its enablement. Specifically, the following references, which are provided in the Information Disclosure Statement included herewith, clearly demonstrate the prophylactic and therapeutic effects of neutralizing antibodies against SARS infection.

1. ter Meulin, et.al. (Human monoclonal antibody as prophylaxis for SARS coronavirus infection in ferrets. Lancet. 2004 Jun 26;363(9427):2139-41). The authors investigated prophylaxis of SARS coronavirus infection with a neutralizing human monoclonal antibody in ferrets, which can be readily infected with the virus. Prophylactic administration of the monoclonal antibody at 10 mg/kg reduced replication of SARS coronavirus in the lungs of infected ferrets by 3.3 logs, completely prevented the development of SARS coronavirus-induced macroscopic lung pathology, and abolished shedding of virus in pharyngeal secretions. According to the authors, the data generated in this animal model show that administration of a human monoclonal antibody might offer a feasible and effective prophylaxis for the control of human SARS coronavirus infection.

2. Roberts, et. al. (Therapy with a severe acute respiratory syndrome-associated coronavirus-neutralizing human monoclonal antibody reduces disease severity and viral burden in golden Syrian hamsters. J. Infect. Dis. 2006 Mar 1;193(5):685-92). In this study, the authors show that immunotherapy with monoclonal antibodies (MAbs) offers safe intervention for the prevention of infection in patients after organ transplantation and for the treatment of cancers and

autoimmune diseases. MAb 201 is a severe acute respiratory syndrome-associated coronavirus (SARS-CoV)-specific MAb that prevents establishment of viral replication in vitro and prevents viral replication *in vivo* when administered prophylactically. The efficacy of MAb 201 in the treatment of SARS was evaluated in golden Syrian hamsters, an animal model that supports SARS-CoV replication to high levels and displays severe pathological changes associated with infection, including pneumonitis and pulmonary consolidation. The authors conclude, based on this study, that MAb 201 may be useful in the arsenal of tools to combat SARS.

3. Sui, et.al.(Evaluation of human monoclonal antibody 80R for immunoprophylaxis of severe acute respiratory syndrome by an animal study, epitope mapping, and analysis of spike variants. J. Virol. 2005 May;79(10):5900-6). In this report, the antiviral activity of 80R immunoglobulin G1 (IgG1), a human monoclonal antibody against severe acute respiratory syndrome coronavirus (SARS-CoV) spike (S) protein that acts as a viral entry inhibitor in vitro, was investigated *in vivo* in a mouse model. When 80R IgG1 was given prophylactically to mice at doses therapeutically achievable in humans, viral replication was reduced by more than 4 orders of magnitude to below assay limits.

These references provide ample experimental evidence of the ability of neutralizing antibodies to inhibit and ameliorate SARS infection *in vivo*. Applicants maintain that in view of (i) the *in vivo* effect of SARS-neutralizing antibodies as demonstrated by these references, (ii) the guidance provided by the specification for making and using the claimed vaccine, and (iii) routine skill at the time of filing, one skilled in the art would have been able to make and use the claimed vaccine without undue experimentation. Thus, applicants maintain that claim 17 satisfies the enablement requirement.

35 U.S.C. §102

The Examiner rejected claims 8-11, 18 and 37-41 under 35 U.S.C. §102 as allegedly anticipated by Li et al. (Genomics, Proteomics and Bioinformatics 1:108-117, May 2003). Claims 9-11, 18 and 37-41 have been cancelled, rendering their rejection moot.

In response to the rejection of claim 8, applicants respectfully traverse.

Again, claim 8, as amended, provides an isolated antibody to the neutralizing fragment of the spike (S) gene of SARS CoV, clone 12 of the 2774 strain (SEQ ID NO:5).

The Examiner asserts, in relevant part, that Li et al. teach the claimed antibody, since "Li teaches SARS patient antibodies which bind to residues 1130-1147 (within SEQ ID NO:5 ...)."

In response, applicants stress that the claimed antibody is *isolated*, and that Li et al. fail to teach an antibody isolation step. Rather, patients' sera were evaluated using an ELISA procedure, without performing an antibody isolation step. Thus, Li et al. fail to anticipate the claimed isolated antibody.

The Examiner also rejected claims 8-11, 13, 17, 18, 20, 37-41, 43, 46 and 48 under 35 U.S.C. §102 as allegedly anticipated by Dmitrov et al. (WO 2005/010034). Claims 9-11, 18, 20, 37-41, 43, 46 and 48 have been cancelled, rendering their rejection moot.

In response to the rejection of claims 8, 13 and 17, applicants respectfully traverse.

Amended claim 8, providing an isolated antibody, is discussed above. Claims 13 and 17 provide a kit and vaccine, respectively, and each depends from claim 8.

The Examiner asserts, in relevant part, that Dmitrov et al. teaches the claimed antibody, kit and vaccine. In support, the Examiner notes the many pages of Dmitrov containing what appears to applicants to be a "shot gun"-type listing of spike protein fragments (including, e.g.,

SEQ ID NO:31 (aa 1101-1189)) far exceeding those actually studied by Dmitrov et al., as well as antibodies to those fragments and related compositions and kits.

In response, applicants stress that the claimed antibody is *isolated*, and that the Examiner has not shown how Dmitrov et al. teaches the isolated antibody of claim 8. As claims 13 and 17 each depend from claim 8, these claims require that the antibody in the kit and vaccine, respectively, be isolated. The Examiner has not shown how Dmitrov et al. teach this kit or vaccine. Thus, Dmitrov et al. fail to anticipate the claimed isolated antibody, kit and vaccine.

35 U.S.C. §103

The Examiner rejected claims 13, 20 and 43 under 35 U.S.C. §103 as allegedly anticipated by, or in the alternative, obvious over Li et al. Claims 20 and 43 have been cancelled, rendering their rejection moot.

In response to the rejection of claim 13, applicants respectfully traverse.

Again, claim 13 provides a kit comprising the isolated antibody of claim 8. Li et al. is discussed above, as is the Examiner's understanding of this reference. For emphasis, however, it is again stressed that this reference teaches the evaluation of patients' sera using an ELISA procedure, *without* performing an antibody isolation step. Li et al. therefore fails to anticipate the claimed kit for the same reason this reference fails to anticipate the claimed isolated antibody.

With respect to obviousness, applicants further point out that Li et al., alone or in combination with routine skill, do not teach or suggest all elements of the claimed kit, namely, the presence of the particular isolated antibody of claim 8. Since such teaching a suggestion is absent, applicants maintain that the Examiner has not properly demonstrated obviousness of claim 13.

In view of the above, applicants maintain that claim 13 satisfies the requirements of 35 U.S.C. §103.

INFORMATION DISCLOSURE STATEMENT

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Form PTO/SB/08a. Copies of the listed documents are also enclosed.

It is respectfully requested that these documents be considered by the Examiner, and that the copy of the enclosed Form PTO/SB/08a be returned indicating that such information has been considered.

In accordance with 37 C.F.R §§1.97(g) and (h), the filing of this Information Disclosure Statement should not be construed as a representation that a search has been made or that information cited is, or is considered to be, material to patentability as defined in §1.56(b), or that any cited document listed or attached is (or constitutes) prior art. Unless otherwise indicated, the date of publication indicated for an item is taken from the face of the item and Applicants reserve the right to prove that the date of publication is in fact different.

If any additional fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
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